

#### REMARKS

Claims 1-6, 8-20, 29-40, and 58-66 are pending in the application. Claims 1, 8, 13, and 29 have been amended herein. The amendment to claims 1, 8, and 29 is supported by disclosure at page 17, line 30 to page 23, line 4 of the specification. The amendment to claim 13 is supported by the claims as originally filed. New claims 58-66 have been added. New claims 58-60 are supported by the claims as originally filed and by disclosure at page 18, line 19 of the specification. New claims 61, 63, and 65 are supported by the claims as originally filed and by disclosure at page 9, line 15 of the specification. New claims 62, 64, and 66 are supported by the claims as originally filed and by disclosure at page 10, line 1 of the specification. Thus, no new matter has been added.

In the Office Action dated October 21, 2002, the Examiner acknowledged that all rejections had been overcome except for obviousness-type double patenting. The Examiner also indicated that a timely filed terminal disclaimer would overcome such rejections. Accordingly, applicants submit herewith such a terminal disclaimer and thus believe all rejections have been overcome. Additionally, applicants amend herein some of the claims for clarity purposes. These amendments are discussed below.

Claims 1, 8, and 29 have been amended to particularly point out and distinctly claim the instant invention. Applicants have amended these claims to specifically recite the alleles of the IL-1 33441461 and IL-1 44112332 inflammatory haplotypes. Rather than reciting a plurality of alleles from a haplotype selected from the group consisting of an IL-1 44112332 and IL-1 33441461 haplotypes, the claims as amended now recite that detection is of one or more of the alleles from those haplotypes, with each allele specifically recited except for allele 2 of the VNTR marker of IL-RN. Applicants realize that the claims had been previously amended from reciting "at least one allele of the haplotype" to reciting "plurality of alleles". Applicants submit that the claims as presented herein, including the recitation of "one or more" are patentable over prior art, because none of the alleles as recited in claim 1 have been disclosed in the art as being associated with a disease or condition associated with an IL-1 inflammatory haplotype. In the prior prosecution, the Examiner's position was that the association between allele 2 of the IL-1RN polymorphic allele and an IL-1 inflammatory haplotype disease or condition had been disclosed. See Office Action mailed March 29, 2002, at page 8. This allele, allele 2 of the

VNTR marker of IL-1RN, is no longer recited in claim 1. Therefore, applicants believe that claim 1 is patentable.

Additionally, new claims 58-60 recite methods directed to the further detection of allele 2 of the VNTR marker of IL-1RN. Therefore, methods using this marker require that 2 or more alleles be detected. Applicants assert that claims 1, 8, and 29, as amended, and new claims 58-60 do not go beyond the scope of claims 1, 8, and 29 as presented in Applicant's Response and Amendment dated September 30, 2002.

New claims 61 and 62 recite methods directed to detecting whether a subject is suffering from or is predisposed to developing a cardiovascular disease or osteoporosis. New claims 63 and 64 recite methods directed to selecting an appropriate therapeutic for an individual that is suffering from or is predisposed to developing a cardiovascular disease or osteoporosis. New claims 65 and 66 recite methods directed to treating or preventing the development of a cardiovascular disease or osteoporosis in a subject. Applicants assert that new claims 61-66 do not go beyond the scope of claims 1, 8, and 29 as presented in Applicant's Response and Amendment dated September 30, 2002.

#### **Double Patenting**

The only remaining rejection from the October 21, 2002 Office Action is that of obviousness-type double patenting. Claims 1-6, 8-20, and 29-40 remained rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 8-57 of United States Patent Number 6,268,142.

In order to facilitate the prosecution of this application, Applicants submit herewith a terminal disclaimer over U.S. Patent Number 6,268,142. Thus, this rejection of these claims is now moot and should be withdrawn.

Applicants: Duff *et al.*  
U.S.S.N.: 09/845,129

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance, and a Notice of Allowance is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Janine M. Susan

For R. Elrifi, Reg. No. 39,529  
Janine M. Susan, Reg. No. 46,119  
c/o MINTZ, LEVIN, COHN, FERRIS,  
GLOVSKY AND POPEO, P.C.  
One Financial Center  
Boston, Massachusetts 02111  
Tel: (617) 542-6000  
Fax: (617) 542-2241

Dated: July 8, 2003